REMARKS

Claims 1 and 3-20 are pending in the instant application. Claims 5-20 are withdrawn from consideration. Claims 1, 3, and 4 are rejected. Claim 1 has been amended. The amendment is supported throughout the application, for example in paragraphs 28 and 53. The specification has been amended to correct obvious typographical errors. The amendment is supported, for example, in paragraph 73 and in the titles of the tables. The abstract has been amended to place it on a separate page after the claims. The abstract is a copy of the abstract filed with the application. No amendment is made other than the location of the abstract in the application. The amendments adds no new matter.

Election/ restriction requirement made final

The Office Action notes that the election/ restriction requirement has been made final and that each of the inventions set forth in the restriction requirement is a separate invention.

Claim 1 has been amended as set forth above to confirm the election made by Melissa Hunter-Ensor in the telephonic interview on September 11, 2007. Claim 1 is drawn to detection of a polymorphism at -1082 in IL-10. Claim 3 is drawn to detection of a polymorphism at -1082A in IL-10, at -174C for IL-6, and ApoE4 carrier status. Claim 4 is drawn to detection of a polymorphism at -1082A in IL-10, at -174C for IL-6, ApoE4 carrier status, and 1082A of IL-1.

Objection to the drawings

The drawings have been objected to for not describing what the lanes in Figure 2 represent. Applicant respectfully disagrees. The legend for Figure 2 reads as follows:

FIG. 2 shows paradigmatic example of IL-10 genotyping for six different samples. In each gel the heaviest bands correspond to the amplicons of the human beta-globin gene which is used as the internal controls. The other specific amplified DNA fragments correspond to the polymorphisms of the IL-10 gene: GCC/GCC (A), GCC/ACC (B), GCC/ATA (C), ACC/ACC (D), ACC/ATA (E), ATA/ATA (F), and

Each of the lanes represents a different sample. The specific identity of the samples is not relevant. The invention is based on a population analysis, not the particular characteristics of any single sample. The polymorphism detected in each group is clearly indicated by the figure legend. Applicant submits that no further labeling or identification of the lanes is required. Withdrawal of the rejection is respectfully requested.

Failure of Information Disclosure Statement to Comply with 37 C.F.R. §1.98(a)(2)

The Office Action states that the IDS filed fails to comply with the requirements of 37 C.F.R. §1.98(a)(2) for not providing a legible copy of each of the non-patent literature publications listed. Applicant notes that the Examiner has initialed each of the references listed in the IDS as having been considered. Applicant requests that the Examiner specifically identify any references required so that the Applicant can provide them accordingly.

Objection to the Specification

The Office Action states that the application does not contain an abstract of the disclosure as required by 37 C.F.R. 1.72(b). Applicant submits that an abstract was filed and is published with the application (see US Patent Publication 20050260767). Applicants have indicated an amendment to the specification as set forth above and provided a substitute sheet attached at the end of the amendment providing the abstract

as filed on a separate sheet marked as a substitute sheet. No new matter is added. Withdrawal of the rejection is respectfully requested.

Rejections for lack of enablement under 35 U.S.C. §112, ¶1

The Office Action has rejected claims 1 and 3-4 for failing to comply with the enablement requirement. Applicant respectfully disagrees.

Claim 1 is amended as set forth above to relate to a method that is useful or predictive for a predisposition to Alzheimer's disease or diagnostic of Alzheimer's disease. The Office Action cites multiple references, both prior art and post-published to support the position that "A method of determining..." Alzheimer's disease is known to be unpredictable. However, there is literature which confirms the study upon which the present application is based. Therefore, despite what the Office Action has asserted the gene polymorphisms are still highly determining of the presence or absence of a predisposition to develop Alzheimer's disease. See, for example, Combarros et al *J. Neural Transm.* **2008** Jun:115 (6) pp 863-7 (Epub 2008 Feb 26) "Aromatase and interleukin-10 genetic variants interactively modulate Alzheimer's disease risk." or SL Ma et al *Neurobiol Aging* **2005** Jul: 26(7) pp 1005-10 (epub 2004, Nov 23) "The Association Between Promoter Polymorphism of the Interleukin-10 gene and Alzheimer's disease." or Infante et al. *Neurology.* **2004**; 63: pp1135-1136 "Gene–gene interaction between interleukin-6 and interleukin-10 reduces AD risk" (copies enclosed).

Without agreeing with the Office Action and purely to progress the prosecution of the application, Applicant has amended the preamble of the claim to refer to a method that is useful or predictive in determining a predisposition or as a diagnostic, rather than an absolute diagnosis. Applicant asserts that such a method is fully enabled and such an amendment is fully supported by the application as filed. Withdrawal of the rejection is respectfully requested.

The Office Action on page 7 of the Office Action requests clarification of whether Table 1 refers to a "...comparison of all alleles of AD to healthy control or specific individual allele of AD to healthy control..." (*sic*). Applicant submits that it is evident from the text introducing Table I that all of the genotypes and hence all of the alleles of AD are compared against healthy controls.

Applicant thanks the Examiner for the careful reading of the specification and noting the incorrect references to tables in the specification. Applicant has amended the necessary paragraph on page 16 as set forth above to correct obvious typographical errors. Table II is entitled "IL-10 genotype distribution and age at onset Genotype." Table III is entitled "IL-10 genotype distribution and MMSE Genotype." The amendments to the specification are made to point the reader to the correct table related to age or cognitive function. The amendments contain no new matter.

On page 8, the Office Action inquires how more alleles than patients can be included the figures in Tables V and VI when referring to alleles as only 65 patients and 65 controls were tested. Applicant notes that each genotype refers to 2 alleles so that in Table V the numbers are made up as follows:-

	Genotype			Allele	
	G/G (H)[a]	G/A (M)	A/A (L)	A	G
AD	4 (6.4%)	28 (44.4%)	31 (49.2%)	90 (71.4%) [90=28+31+31]	36 (28.6%) [36=28+4+4]
HC	14 (22.2%)	29 (46%)	20 (31.8%)	69 (54.8%) [69=20+20+29]	57 (45.2%) [57=14+14+29]

Six patients could not be reliably typed (4AD and 2 HC) because insufficient numbers of cells were obtained.

Similarly, in Table VI the numbers are made up as follows:-

	Genotype			Allele	
	G/G (H)[a]	G/C(M)	C/C (L)	C	G
AD	17 (29%)	34 (57.6%)	8 (13.4%)	50 (42.4%) [50=34+8+8]	68 (57.6%) [68=17+17+34]
HC	32 (50%)	27 (42.2%)	5 (7.8%)	37 (28.9%) [37=27+5+5]	91 (71.1%) [91=32+32+27]

Again, six patients could not be reliably typed (4AD and 2 HC) because insufficient numbers of cells were obtained.

Claim 1 as filed herewith is also restricted to a human subject.

In view of the forgoing amendments and remarks, withdrawal of the rejections for lack of enablement is respectfully requested.

Rejection for lack of clarity under 35 U.S.C. §112, ¶2

Claims 1 and 3-4 have been rejected for being indefinite and failing to particularly point out and distinctly claim the method of the invention. The final process step of the claim now recites the method set forth in the preamble. In view of the amendment, Applicant submits that the claim is definite. Withdrawal of the rejection is respectfully requested.

Rejection for anticipation under 35 U.S.C. §102(b)

Claims 1 and 3-4 have been rejected for anticipation in view of each Scola et al. and Wang et al. Applicant respectfully disagrees.

Neither Scola nor Wang teach or suggest that specific alleles of IL-10 are associated with a predisposition or the presence of Alzheimer's disease as claimed. Withdrawal of the rejections is respectfully requested.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Dated: July 15, 2008

Respectfully submitted,

By /Colleen McKiernan/
Colleen McKiernan, Ph.D.
Registration No.: 48,570
EDWARDS ANGELL PALMER & DODGE LLP
P.O. Box 55874
Boston, Massachusetts 02205
(617) 517-5555
Attorneys/Agents For Applicant